Seattle, WA; [4] Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA; [5] Transplantation Biology, Fred Hutchinson Cancer Research Center, Seattle, WA; [6] Clinical Research Division, Fred Hutchinson Cancer Research Center (FHCRC), Seattle, WA; [7] Fred Hutchinson Cancer Research Center, Seattle, WA; [8] Laboratory Medicine & Pathology, University of Washington, Seattle, WA; [9] Fred Hutchinson Cancer Rsrch Ctr, Seattle, WA

Background: Allogeneic HCT is used commonly in adults with ALL. MRD is an accepted prognostic factor in ALL. Being MRD-negative (MRD^{Neg}) overcomes age and cytogenetics (CG; Bassan, *Blood*, 2009), and it is predictive of outcome without (No) HCT and prior to myeloablative (MAC) and reduced-intensity HCT (RIC). However, comparisons of these treatments in this favorable-risk subgroup are limited. We sought to examine outcomes with these 3 approaches exclusively in pts in first MRD^{Neg} remission (MRD^{Neg} CR1).
Methods: We performed a retrospective analysis of pts that were diagnosed or referred for HCT at our Center since 2005. MRD^{Neg} was defined as undetectable by all methods used: Multiparameter flow cytometry was used in all pts, though other measures (PCR, FISH, and/or CG) were considered if performed. Clinical risk factors at diagnosis (dx) included age $\geq$ 35, high white blood count (WBC; $>$ 30 in B-ALL, $>$ 100 in T-ALL), and adverse CG (Ph+, low hypodiploid/near triploid, complex [$\geq$ 5 abnormalities], MLL rearranged, t[8;14], -7, and +8). Group characteristics were compared with Fisher's exact test. Kaplan-Meier plots and Cox proportional hazard models were used to investigate associations between variables.
Results: Of 127 pts identified, 53 (42%) received MAC, 19 (15%) received RIC, and 55 (43%) No HCT while in MRD^{Neg} CR1. RIC pts were significantly more likely than MAC and No HCT pts to be $\geq$ 35 years old at dx (89% vs 60% vs 51%, respectively [resp.]; P = 0.0084) and have adverse CG (83% vs 53% vs 30%, resp.; P < 0.001). There were no significant differences in WBC at dx, initial therapy received, or (among the HCT groups) stem-cell donor or product. All Ph+ pts received tyrosine kinase inhibitors.

Overall survival (OS) from dx in these 3 groups was similar (P = 0.35; Fig 1), though relapse was significantly less with MAC (P = 0.01; Fig 2). 3-year (yr) estimates of OS with MAC, RIC, and No HCT were 71%, 73%, and 75% (resp.), and 30%, 51%, and 60% (resp.) for relapse. 3-yr non-relapse mortality was 17% with MAC vs 5% with RIC (P = 0.15). Compared to No HCT, the risk of death was not different with MAC

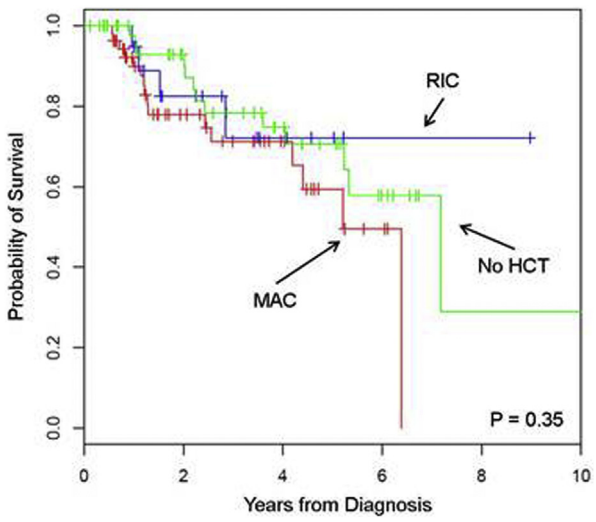

Fig 1. OS from diagnosis among pts in **MRD^{Neg} CR1**.

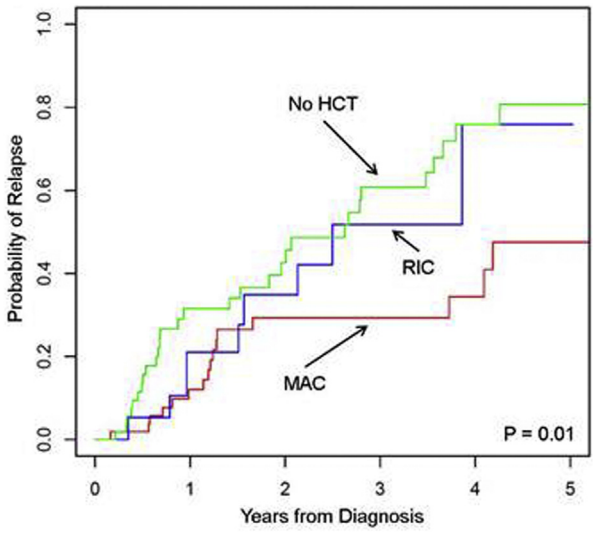

Fig 2. Cumulative incidence of relapse among pts in MR^{Neg} CR1 (competing risk is death before relapse).

(hazard ratio [HR] 1.6, P = 0.19) or RIC (HR 1.0, P = 1.0), adjusted for WBC. However, relapse was lower with HCT, adjusted for WBC and (due to more events) adverse CG: significantly so after MAC (HR 0.35, P = 0.0014) but not with RIC (HR 0.57, P = 0.18). OS was also similar with Ph+ and Ph- studied separately (P = 0.99 and 0.14, resp.).

In a distinct analysis of 23 pts who underwent HCT while MRD^{Neg} beyond CR1 (CR2+), OS from HCT was comparable for CR1 and CR2+ (P = 0.46). 3-yr estimates of OS were 69% and 62% (resp.).
Conclusions: Among contemporary adults with ALL in MRD^{Neg} CR1, RIC pts were more commonly older with adverse CG. MAC yielded significantly less relapse, but OS was no different than with RIC or No HCT. HCT while MRD^{Neg} yields similar outcomes in CR1 and CR2+. For pts in MRD^{Neg} CR1, the role of up-front HCT is less clear.

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Minimal Residual Disease By PCR Testing Is a Significant Predictor of Disease Relapse in Patients with FLT3 Positive AML after Hematopoietic Stem Cell Transplantation

Sameh Gaballa [1], *Rima Saliba* [1], *Betul Oran* [1], *Jonathan E. Brammer* [1], *Julianne Chen* [1], *Gabriela Rondon* [1], *Amin M. Alousi* [1], *Partow Kebriaei* [1], *Uday R. Popat* [1], *Borje S. Andersson* [1], *Elizabeth J. Shpall* [1], *Elias Jabbour* [2], *Naval Daver* [2], *Michael Andreeff* [2], *Farhad Ravandi* [2], *Jorge Cortes* [2], *Richard E. Champlin* [1], *Stefan O. Ciurea* [1]. *[1] Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, TX; [2] Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX*

Introduction: FLT3 mutations are present in up to 30% of AML pts with diploid cytogenetics. Allogeneic hematopoietic stem cell transplantation (AlloSCT) has emerged as the preferred therapy for this high-risk group, but these pts remain at high risk for disease relapse. The significance of FLT3 detection by PCR, as a minimal residual disease marker, at the time of AlloSCT remains unclear and little is known about the risk factors associated with risk of relapse among FLT3 AML pts.
Methods: We reviewed 1255 AML pts who underwent first AlloSCT between 2000 and 2014, and identified 200 adult pts with a FLT3-ITD or FLT3-TKD mutation found at diagnosis

Table 1

Sex (M/F)	98/102
Median age	51 (18-72)
Age > 50	53%
KPS > 80%	64%
HCT-CI Score >4	19%

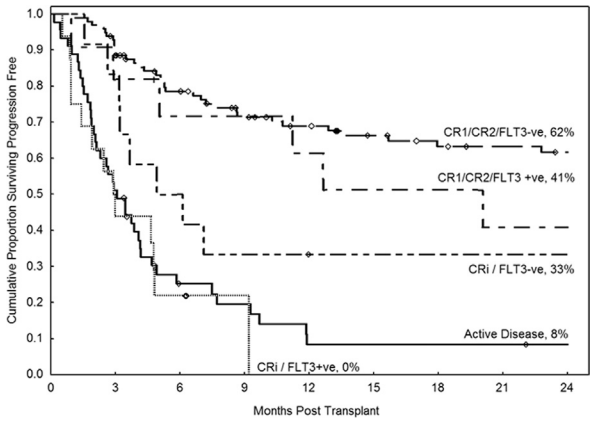

Figure 1A. Progression-free survival.

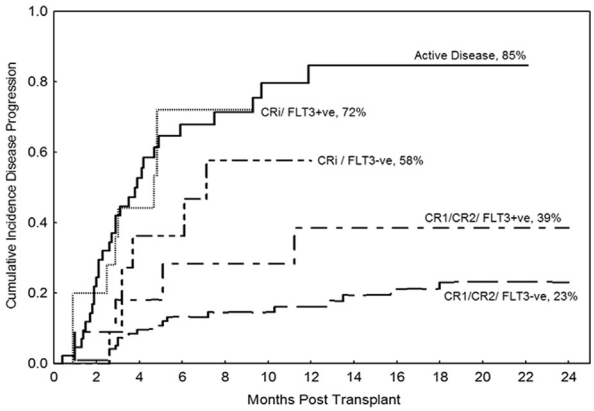

Figure 1B. Cumulative incidence of relapse for *FiT3+ve* pts by disease status at transplant.

(Table1). All donor sources were included: 63 matched sibling (MSD), 95 10/10 MUD, 11 9/10 MUD, 18 cord blood (CB), and 13 haploidentical (Haplo).

Results: The majority of pts received myeloablative conditioning (n=170; busulfan-based n=148). Disease status at AlloSCT was: CR1 (n=99), CR2 (n=20), CR with incomplete count recovery or hypoplastic marrow or CR3 (CRi; n=31), and active disease (AD; n=50). Thirty percent of pts received a FLT3 inhibitor before AlloSCT. After a median follow-up of 27 mo, the 2-year (2Y) OS and PFS rates were 43% and 41%, respectively. Relapse-related mortality was the main cause of death (68%). Remission and FLT3 status at the time of AlloSCT were significantly associated with PFS. Compared to CR1 pts, PFS was not different in CR2 [HR 1.5, p=0.3], but it was worse in CRi (HR 3.9, p<0.001) and AD pts (HR 5.9, p<0.001). The 2Y PFS was highest in CR1/2 FLT3−ve pts (62%) compared to the other groups: CR1/2 FLT3+ve (41%, p=0.3); CRi FLT3−ve (33%, p=0.01); CRi FLT3+ve (0%, p<0.001); AD (8% p<0.001) (Figures 1A, 1B). On multivariate analysis, independent predictors of worse PFS included: AD [HR 4.5, p<0.001], CRi FLT3+ve [HR 7.2, p<0.001], KPS≤80 [HR2.1, p<0.001], HCT-CI>4 [HR 1.6, p=0.05], and unrelated donor source [HR 1.6, p=0.05]. No difference in PFS was found between Haplo and MSD donor sources (HR=0.9, p=0.9). No significant association was identified by age, conditioning intensity or use of a FLT3 inhibitor prior to transplant. Post-transplant FLT3 status was available for 105 of 190 evaluable pts by day 30. Among them, 7 pts had detectable FLT3 PCR and 5/7 pts (71%) relapsed.

Conclusion: Morphologic remission and FLT3 PCR status at the time of transplant are key predictors of relapse risk in pts with FLT3+ AML. Patients who achieved a morphologic CR with an undetectable FLT3 by PCR at the time of SCT had the best outcomes and should undergo an AlloSCT without delay. Although the experience is limited, Haplo transplants had similar outcomes to MSD transplants. Prospective clinical trials with FLT3 inhibitors post-transplant are warranted at least for pts with AD or persistent FLT3+ on PCR at transplant.

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Comparing the Results of Non-TBI Hematopoietic Stem Cell Transplantation in Pediatric Patients with Acute Lymphoblastic Leukemia (ALL) with and without CNS Involvement

Amir Ali Hamidieh, *Maryam Kabootari, Mohsen Esfandbod, Maryam Behfar, Arash Jalali, Ardeshir Ghavamzadeh.*
Hematology, Oncology and Stem Cell Transplantation Research center, Tehran University of Medical Sciences, Tehran, Iran

Introduction: There are limited data on the impact of hematopoietic stem cell transplant (HSCT) conditioning regimen, especially without total body radiation (TBI) in pediatric patients with acute lymphoblastic leukemia (ALL) with central nervous system (CNS) involvement. The aim of this study is compare the results of HSCT using non-TBI conditioning regimen in ALL patients aged ≤18 years with or without CNS involvement.

Patients and Methods: Records of 183 patients with ALL (128 male; 55 female) with a median age of 14.1±3.7 years who had undergone HSCT were studied and classified in two groups: with and without CNS involvement. Long-term consequence of the HSCT consisting of leukemia free survival (LFS), the overall survival (OS), relapse and transplant-related mortality (TRM) was compared in the two groups.

Results: A total of 183 ALL patients (148 without CNS involvement and 35 with CNS involvement) underwent HSCT in our center using a TBI-free conditioning containing Busulfan and Cyclophosphomide. The median time of follow up was 42.1 months. Estimated probability on relapse at 4 year was 51.4% in patients with CNS involvement and 42.1% in patients without CNS involvement (p=0.588). Regarding survival analysis, 4-year OS and LFS in all patients was 44.4% (SE:2.5%) and 39.7%(SE:2.5%). In multivariate analysis there were no significant differences in OS and LFS between two groups (p=0.839, p=894) nor was there a difference in relapse probability (HR:1.20, 95%CI:0.69-2.1, p=0.513) and TRM (HR:0.44, 95%CI:0.10-1.92, p=0.286).

Conclusion: HSCT using a non TBI conditioning regimen in ALL are similar with studies using TBI containing regimens. Furthermore HSCT leads to similar clinical outcomes and long-term survival in the ALL pediatric patients with or without CNS involvement.

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Safety and Efficacy of Ibrutinib in Patients with Relapsed/Refractory (R/B) Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Who Have Undergone Prior Allogeneic Stem Cell Transplant

David B. Miklos [1], *Steven Coutre* [2], *Susan O'Brien* [3], *John C. Byrd* [4], *Peter Hillmen* [5], *Jennifer R. Brown* [6], *Martin Dyer* [7], *Anthony R. Mato* [8], *Michael Keating* [3], *Cathy Zhou* [9], *Maria Fardis* [9], *Lori Styles* [9], *Samantha Jaglowski* [4]